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# Palladium-Catalyzed Intramolecular Diamination of Acrylic Esters Using Sulfamates as Nitrogen Source

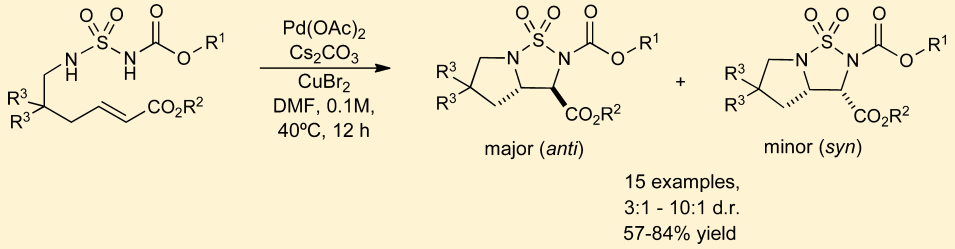
Patricia Chávez,[†] Jonathan Kirsch,[†] Jan Streuff,[‡] and Kilian Muñiz*[,†,§]

[†]Institute of Chemical Research of Catalonia (ICIQ), Av. Països Catalans, 16, E-43007 Tarragona, Spain

[‡]Albert-Ludwigs-Universität Freiburg, Albertstr. 21, 79104 Freiburg, Germany

[§]Catalan Institution for Research and Advanced Studies (ICREA), Pg. Lluís Companys 23, 08010 Barcelona, Spain

Supporting Information




**ABSTRACT:** An intramolecular diamination of acrylates is reported using sulfamates as nitrogen sources. This reaction proceeds under palladium(II) catalysis with copper bromide as oxidant and gives rise to *anti*-configured 2,3-diamino carboxylates as bicyclic sulfamate derivatives. An aminobrominated intermediate within the diamination reaction was isolated that allowed to clarify the reaction mechanism and to rationalize the observed preferential product stereochemistry.

## INTRODUCTION

The 2,3-diamino carboxylic acid motif represents an interesting nonproteinogenic amino acid[1] that has attracted attention for its presence in biologically active compounds.[2] Mannich-type reactions under transition-metal catalysis or organocatalysis have been described as particularly suitable approaches to this class of compounds.[3]

Oxidative metal catalysis for diamination of alkenes has recently emerged as a powerful tool for the synthesis of heterocycles that incorporate the vicinal diamine structural motif.[4] Reactions to this end include palladium,[5] nickel,[6] gold,[7] and copper[8] catalysis.[9,10] Within this context, some time ago we reported the diamination of acrylates using ureas as nitrogen sources (Scheme 1).[11]

This reaction proceeds under palladium catalysis with copper bromide as terminal oxidant and allows us to selectively generate *syn*-configured 2,3-diamino esters. One of these compounds served as building block in the synthesis of the natural product absouline.

## RESULTS AND DISCUSSION

We now became interested in the use of the corresponding sulfamates as nitrogen sources, which are more conveniently accessible and usually show a broader potential for structural diversification. They were already employed in oxidative diamination reactions of terminal alkenes using nickel catalysis.[6] Herein, we describe the application of intramolecular diamination of acrylates using sulfamate groups as nitrogen source.

Starting materials **2** are available from cross-metathesis between alkyl acrylate and previously described $\omega$-alkenyl sulfamides (Scheme 2).[6] The reaction employs an excess of the corresponding acrylate leading to fumarate as an easily removable byproduct.

After some experimentation, conditions were found under which the diamination reaction of **2a** to cyclized **3a** proceeded under palladium catalysis with high yield and good diastereoselectivity. Initial attempts to employ high oxidation state catalysis[12] and acetate base did not meet with success (Table 1, entry 1). Instead, use of copper bromide as oxidant resulted more convenient (entry 2). Solvent exploration revealed DMF to be superior than dichloromethane or THF, respectively (entries 2−4). Further optimization addressed the nature of base and cesium carbonate was identified as optimum base in comparison to acetate and hydrogenphosphate (entries 4−6). Complete conversion was observed for a reaction at slightly enhanced temperature of 40 °C (entry 7). This optimization process hence identified cesium carbonate as optimum base and DMF as best solvent generating product **3a** in 83% isolated yield. No reaction was observed in the absence of a palladium catalyst (entry 8). As a usual feature in the intramolecular diamination under palladium catalysis,[5a−d,6] the presence of base is required (entry 9).

Under the optimized conditions, the diamination reaction of **2a** reaches full completion, and an overall yield of 83% (76% for **3a** and 7% for **4a**) is obtained. The high yield of **3a** is

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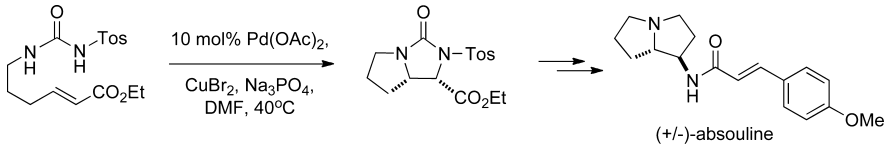
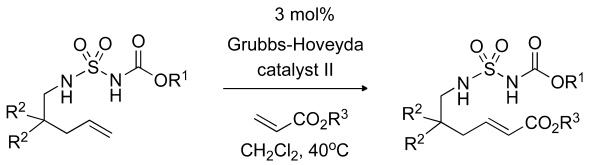
**Scheme 1**




**Scheme 2. Metathesis Approach to Starting Materials 2**




**1a**: $R^1$ = Me, $R^2$ = Ph
**1b**: $R^1$ = Bn, $R^2$ = Ph
**1c**: $R^1$ = Bn, $R^2$ = Ph
**1d**: $R^1$ = *t*Bu, $R^2$ = Ph
**1e**: $R^1$ = *t*Bu, $R^2$ = Ph
**1f**: $R^1$ = Bn, $R^2$ = Ph
**1g**: $R^1$ = Me, $R^2$ = Ph
**1h**: $R^1$ = Bn, $R^2$ = H
**1i**: $R^1$ = Me, $(R^2)_2$ = $(CH_2)_5$
**1j**: $R^1$ = *i*Pr, $(R^2)_2$ = $(CH_2)_5$
**1k**: $R^1$ = *t*Bu, $(R^2)_2$ = $(CH_2)_5$
**1l**: $R^1$ = *t*Bu, $(R^2)_2$ = $(CH_2)_5$
**1m**: $R^1$ = *t*Bu, $R^2$ = Me
**1n**: $R^1$ = *t*Bu, $R^2$ = Me
**1o**: $R^1$ = *t*Bu, $R^2$ = *i*Pr

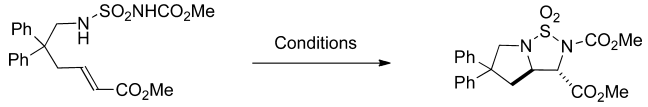
**2a**: $R^1$ = Me, $R^2$ = Ph, $R^3$ = Me, 94%
**2b**: $R^1$ = Bn, $R^2$ = Ph, $R^3$ = *t*Bu, 87%
**2c**: $R^1$ = Bn, $R^2$ = Ph, $R^3$ = Et, 85%
**2d**: $R^1$ = *t*Bu, $R^2$ = Ph, $R^3$ = *t*Bu, 87%
**2e**: $R^1$ = *t*Bu, $R^2$ = Ph, $R^3$ = Me, 89%
**2f**: $R^1$ = Bn, $R^2$ = Ph, $R^3$ = Me, 92%
**2g**: $R^1$ =Me, $R^2$ = Ph, $R^3$ = *t*Bu, 88%
**2h**: $R^1$ = Bn, $R^2$ = H, $R^3$ = Me, 72%
**2i**: $R^1$ = Me, $(R^2)_2$ = $(CH_2)_5$, $R^3$ = *t*Bu, 87%
**2j**: $R^1$ = *i*Pr, $(R^2)_2$ = $(CH_2)_5$, $R^3$ = *t*Bu, 82%
**2k**: $R^1$ = *t*Bu, $(R^2)_2$ = $(CH_2)_5$, $R^3$ = *t*Bu, 87%
**2l**: $R^1$ = *t*Bu, $(R^2)_2$ = $(CH_2)_5$, $R^3$ = Me, 81%
**2m**: $R^1$ = *t*Bu, $R^2$ = Me, $R^3$ = Me, 94%
**2n**: $R^1$ = *t*Bu, $R^2$ = Me, $R^3$ = Et, 82%
**2o**: $R^1$ = *t*Bu, $R^2$ = *i*Pr, $R^3$ = Me, 86%

particularly remarkable in view of the lower yielding trans-formation of parent terminal alkenes **1** under similar conditions.[11] The observed coupling constant of $^3J$ = 4 Hz between the two hydrogen atoms at the newly formed tetrahedral carbon atoms suggested that the reaction leads to preferential formation of a *trans*-configured diamination product **3a**. The corresponding *cis*-isomer **4a** is the minor product and is generated in less than 10% yield. Both relative configurations were unambiguously assured from X-ray analyses (Scheme 3).[13] This reaction outcome constitutes a noteworthy difference to the one from the previous reactions using ureas as nitrogen source, where the corresponding product was obtained as a single diastereomer displaying *syn*-configuration (Scheme 1).

We had observed in an earlier case of a different palladium catalysis that the carbamate nitrogen of the sulfamate group displays rather low nucleophilic character for a direct C–N bond formation.[6] Assuming a related behavior for the present reaction, we set to investigate potential intermediates by conducting the diamination reaction of **2a** at lower reaction temperature (Figure 1). Indeed, when **2a** was oxidized at room temperature (Scheme 3), the corresponding aminobrominated product **5** was the major product (65% isolated yield) together with **3a** (23%). Compound **4a** was not observed. If formed, its amount was below detection level. Treatment of the isolated aminobrominated intermediate **5** with base in DMF gave the expected product **3a** as single isomer in 92% isolated yield. This reaction outcome suggests that the present diamination reaction proceeds through a catalytic cycle of *syn*-amino-palladation[5b,d,e,14,15] to **A** followed by copper-mediated transient palladium oxidation with concomitant C–Br bond formation.[16] This latter step proceeds with clean $S_N2$ chemistry leading to inversion of configuration at carbon. Subsequent C–N bond formation from **B** under a second inversion of configuration leads to *anti*-**3a**. The minor isomer **4a** is either generated from **B** within a minor pathway of direct C–N bond formation or from **C** within an epimerization of the brominated center.

The reaction is general for a range of different substrates. Table 2 shows representative examples of several sulfamates with variation of backbone substitution, the ester groups and the carbamate group of the sulfamate. All these reactions proceed with good to high isolated yields. An *anti*-configuration was obtained for all major products as judged from the respective $^3J$ coupling constants and confirmed by an additional X-ray analysis of product **3l**. Diastereomeric ratios range from

**Table 1. Optimization of Reaction Conditions**




**2a** **3a**

| entry | conditions | conversion[a] (%) | yield[b] (%) |
|---|---|---|---|
| 1 | 10 mol % $Pd(OAc)_2$, $PhI(OAc)_2$ (1.2 equiv), NaOAc (2 equiv), $CH_2Cl_2$, 30 °C | <10 | nd |
| 2 | 10 mol % $Pd(OAc)_2$, $CuBr_2$ (2 equiv), NaOAc (2 equiv), $CH_2Cl_2$, 30 °C | 40 | 34 |
| 3 | 10 mol % $Pd(OAc)_2$, $CuBr_2$ (2 equiv), NaOAc (2 equiv), THF, 30 °C | 45 | 38 |
| 4 | 10 mol % $Pd(OAc)_2$, $CuBr_2$ (2 equiv), NaOAc (2 equiv), DMF, 30 °C | 60 | 54 |
| 5 | 10 mol % $Pd(OAc)_2$, $CuBr_2$ (2 equiv),$Na_2HPO_4$ (2 equiv), DMF, 30 °C | 70 | 56 |
| 6 | 10 mol % $Pd(OAc)_2$, $CuBr_2$ (2 equiv), $Cs_2CO_3$ (2 equiv), DMF, 30 °C | 75 | 68 |
| 7 | **10 mol % $Pd(OAc)_2$, $CuBr_2$ (2 equiv), $Cs_2CO_3$ (2 equiv), DMF, 40 °C** | **>95** | **83** |
| 8 | $CuBr_2$ (2 equiv), $Cs_2CO_3$ (2 equiv), DMF, 30 °C | 0 | nd |
| 9 | 10 mol % $Pd(OAc)_2$, $CuBr_2$ (2 equiv), DMF, 40 °C | <10 | nd |

[a]Estimated conversion from crude $^1$H NMR data. [b]Isolated yield of combined diastereoisomers after purification (around 10:1 ratio for all cases, major diastereomer **3a** shown).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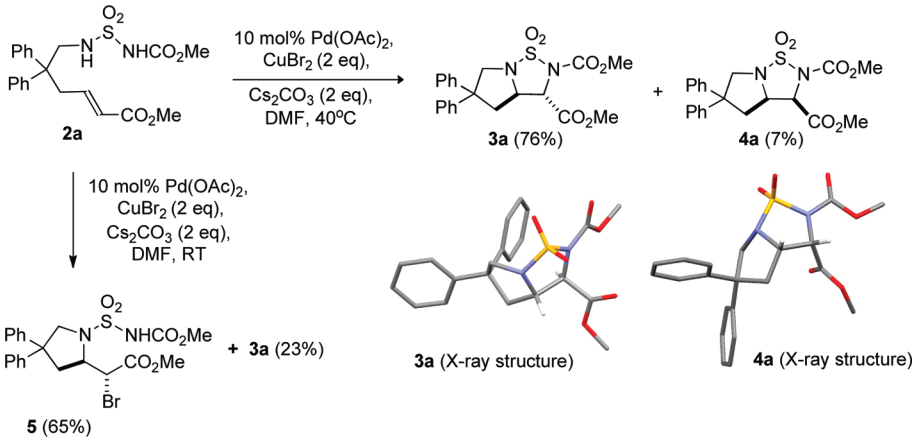
**Scheme 3. Exploration of the Stereochemical Pathways in Diamination of 2a**



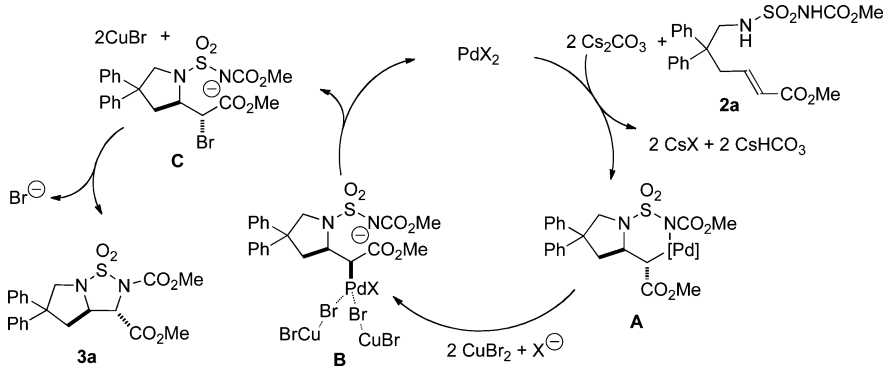




**Figure 1.** Catalytic cycle for Pd-catalyzed diamination of **2a**. X = OAc, Br.

3:1 to 10:1 for reactions that were typically conducted on a 0.2 mmol scale. For the case of **2d** (entry 3), the reaction was performed on a 3 mmol scale, which demonstrated that upscaling does not constitute any problem. It also allowed for isolation and full characterization of the minor diastereomer ***syn*-4d** in this case. Unlike the related case of ureas,[11] cyclization of **2h** without backbone substituents did not suffer any rate decrease or loss of diastereoselectivity, respectively, and the corresponding product **3h** was isolated in 70% yield (entry 7).

**Representative Deprotection and Peptide Coupling.** Since 2,3-diamino carboxylic acids serve as interesting amino acid derivatives, we briefly investigated the general application of products **3** in peptide chemistry. To this end, we found that simple treatment with pyridine in aqueous conditions leads to selective removal of the carbamate groups in compounds **3**.[17] More conveniently, use of KOH in THF−methanol solution cleaves both the carbamate and the ester groups of **3a,f** to arrive at the free carboxylate **6** with intact sulfamate. This aspect should be of interest as it retains the structural rigidity of the *anti*-configured bicyclic system. Coupling of the free acid terminus to the free amine group of an aminoester such as glycine methyl ester under standard conditions[18] furnished the coupling product **7** in 52% yield (Scheme 4).

To summarize, we reported an additional intramolecular diamination reaction that gives rise to 2,3-diamino carboxylic acid building blocks. The use of sulfamates as nitrogen groups allows to generate products with relative *trans*-stereochemistry, which nicely complements an earlier *syn*-stereochemistry using ureas as nitrogen source. Hence, both relative stereochemical arrangements are now available from diamination of easily accessible (*E*)-configured acrylates depending on the nitrogen sources (*trans*-diamines from sulfamates and *syn*-diamines from ureas, respectively).

## EXPERIMENTAL SECTION

**General Procedure for the Formation of the Acrylate Starting Materials.** The terminal alkenes **1** were first synthesized according to a literature protocol.[6] The subsequent formation of the acrylates was done by metathesis reaction under conditions described previously (general procedure A):[11] The respective sulfamate **1** was dissolved in freshly distilled absolute dichloromethane. The respective acrylic ester (8 equiv) was added in one portion via syringe and the resulting solution stirred under nitrogen at room temperature. Grubbs−Hoveyda II catalyst (3 mol %) was added, and the resulting green solution was heated to reflux for a period of 3 h. It was cooled to room temperature and the solvent removed under reduced pressure. Column chromatography (silica gel, EtOAc/hexenes 4:1) gave the corresponding acrylates as white to brown solids.

*(E)-Methyl 6-((N-(Methoxycarbonyl)sulfamoyl)amino)-5,5-diphenylhex-2-enoate (**2a**).* This compound was obtained according to the general procedure A. The subsequent chromatographic purification (hexanes/EtOAc, 3:1) gave 407 mg (0.94 mmol, 94%) of **2a** as a white solid: mp 164−168 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 7.69 (s, 1H), 7.14−7.38 (m, 10H), 6.57 (dt, $J$ = 15.8, 7.4 Hz, 1H), 5.89 (d, $J$ = 15.8 Hz, 1H), 4.65 (t, $J$ = 6.4 Hz, 1H), 3.74 (d, $J$ = 6.4 Hz, 2H), 3.71 (s, 3H), 3.68 (s, 3H), 3.15 (d, $J$ = 7.4 Hz, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 166.5, 151.5, 143.8, 143.6, 128.7, 127.5, 127.2, 124.8, 53.6, 51.5, 50.4, 49.6, 39.4; IR ($cm^{-1}$) 595, 699, 753, 779, 849, 1158, 1272, 1342, 1366, 1471, 1705, 3164, 3262; MS (ESI-TOF) $m/z$ 455.1 [M + Na]$^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{21}H_{24}N_2NaO_6S$ [M + Na]$^+$ 455.1253, found 455.1264.


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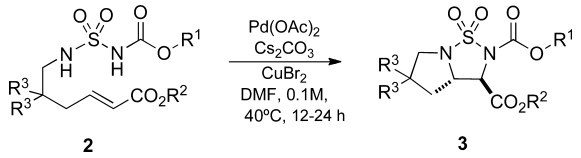
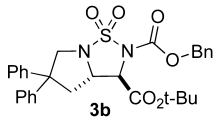
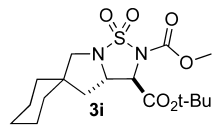
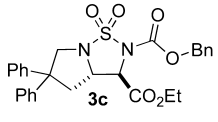
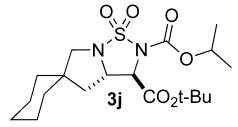
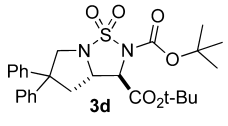
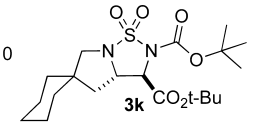
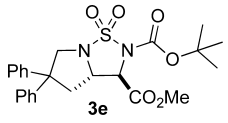
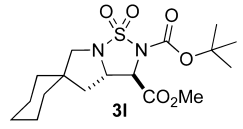
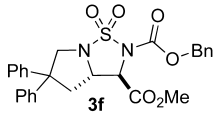
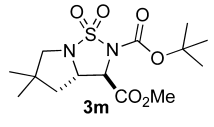
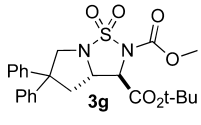
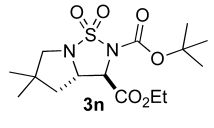
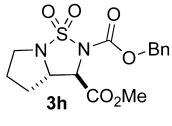
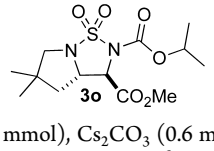
**Table 2. Palladium-Catalyzed Intramolecular Diamination of Acrylates to 1,2-Diamines**[a]

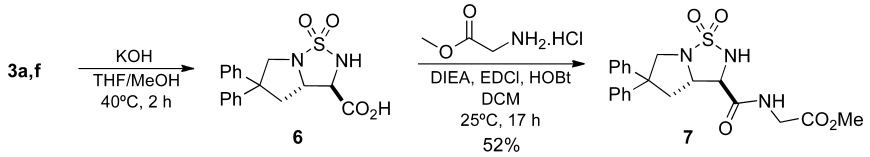



2 → 3

| Entry | Diamination Product | d.r.[b] | Yield [%][c] | Entry | Diamination Product | d.r.[b] | Yield [%][c] |
|---|---|---|---|---|---|---|---|
| 1 |  **3b** | 10:1 | 78 | 8 |  **3i** | 10:1 | 80 |
| 2 |  **3c** | 5:1 | 68 | 9 |  **3j** | 6:1 | 75 |
| 3 |  **3d** | 3:1[d,e] | 57 | 10 |  **3k** | 6:1 | 70 |
| 4 |  **3e** | 8:1 | 72 | 11 |  **3l** | 10:1 | 70 |
| 5 |  **3f** | 10:1 | 84 | 12 |  **3m** | 5:1 | 73 |
| 6 |  **3g** | 6:1 | 76 | 13 |  **3n** | 5:1 | 65 |
| 7 |  **3h** | 4:1 | 70 | 14 |  **3o** | 10:1 | 75 |

[a]General conditions: starting material (0.2 mmol), DMF (2.0 mL), $Pd(OAc)_2$ (0.02 mmol), $Cs_2CO_3$ (0.6 mmol), $CuBr_2$ (0.4 mmol), 40 °C, 12−24 h. [b]Determined by $^1H$ NMR spectroscopy of the crude reaction mixture after reductive workup. [c]Yield of the isolated major product **3** after purification. [d]3 mmol scale up. Isolated yield of major diastereoisomer. The minor diastereoisomer was isolated in 22%. [e]5 mmol scale up. Isolated yield of major diastereoisomer. The minor diastereoisomer was isolated in 29%.

**Scheme 4. Conversion of Diamination Products 3a,f into Dipeptide 6**




*(E)-tert-Butyl 6-((N-((Benzyloxy)carbonyl)sulfamoyl)amino)-5,5-diphenylhex-2-enoate (**2b**).* This compound was obtained according to the general procedure A. The subsequent chromatographic purification (hexanes/EtOAc, 4:1) gave 479 mg (0.87 mmol, 87%) of **2b** as a white solid: mp 104−107 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ = 8.48 (brs, 1H), 7.44−7.02 (m, 15H), 6.61−6.38 (m, 1H), 5.78 (d, $J$ = 15.5 Hz, 1H), 5.10 (s, 2H), 4.72−4.74 (m, 1H), 3.70 (d, $J$ = 6.1 Hz, 2H), 3.06 (d, $J$ = 7.3 Hz, 2H), 1.44 (s, 9H); $^{13}C$ NMR (101 MHz, $CDCl_3$) $\delta$ = 165.5, 151.1, 143.5, 142.5, 134.6, 128.4, 128.3, 128.2, 128.0, 127.4, 126.8, 126.4, 80.1, 68.1, 50.3, 49.4, 39.1, 27.8; IR ($cm^{-1}$) 573, 655, 670, 740, 757, 876, 1071, 1147, 1169, 1238, 1319, 1335, 1429, 1467, 1650, 1705, 2980, 3301; MS (ESI-TOF) $m/z$ 573.2 $[M + Na]^+$ (100); HRMS-ESI-TOF $m/z$ calculated for $C_{30}H_{34}N_2NaO_6S$ $[M + Na]^+$: 573.2051; found: 573.2035.

*(E)-ethyl-6-((N-((benzyloxy)carbonyl)sulfamoyl)amino)-5,5-diphenylhex-2-enoate (**2c**).* This compound was obtained according to the general procedure A. The subsequent chromatographic purification (hexanes/EtOAc, 4:1) gave 444 mg (0.85 mmol, 85%) of **2c** as a white solid. mp: 150−155 °C. $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ = 8.31 (s, 1H), 7.41−6.99 (m, 15H), 6.60 (dt, $J$ = 15.6, 7.4 Hz, 1H), 5.85 (d, $J$ = 15.6 Hz, 1H), 5.11 (s, 2H), 4.72−4.76 (m, 1H), 4.10 (q, $J$ = 7.1 Hz, 2H), 3.71 (d, $J$ = 6.5 Hz, 2H), 3.09 (d, $J$ = 7.4 Hz, 2H), 1.22 (t, $J$ = 7.1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Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 166.1, 151.0, 143.6, 143.5, 134.5, 128.4, 128.4, 128.4, 128.0, 127.4, 126.9, 124.8, 68.1, 60.1, 50.2, 49.4, 39.2, 13.9; IR ($cm^{-1}$) 550, 696, 741, 841, 873, 1068, 1094, 1165, 1195, 1238, 1269, 1332, 1353, 1366, 1426, 1448, 1460, 1654, 1706, 3189, 3294; MS (ESI-TOF) $m/z$ 545.2 $[M + Na]^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{28}H_{30}N_2NaO_6S$ $[M + Na]^+$ 545.1717, found 545.1722.

*(E)-tert-Butyl 6-((N-(tert-Butoxycarbonyl)sulfamoyl)amino)-5,5-diphenylhex-2-enoate (**2d**).* This compound was obtained according to the general procedure A. The subsequent chromatographic purification (hexanes/EtOAc, 4:1) gave 450 mg (0.87 mmol, 87%) of **2d** as a white solid: mp 125−130 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 7.61 (s, 1H), 7.17−7.38 (m, 10H), 6.47 (dt, $J$ = 15.6, 7.4 Hz, 1H), 5.82 (d, $J$ = 15.6 Hz, 1H), 4.61 (t, $J$ = 6.8 Hz, 1H), 3.71 (d, $J$ = 6.8 Hz, 2H), 3.12 (d, $J$ = 7.4 Hz, 2H), 1.46 (s, 9H), 1.42 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 165.5, 149.9, 143.8, 142.4, 128.7, 127.7, 127.2, 126.8, 83.9, 80.2, 50.6, 49.7, 39.5, 28.1, 27.8; IR ($cm^{-1}$) 551, 587, 698, 726, 818, 842, 914, 936, 970, 1077, 1140, 1175, 1250, 1317, 1350, 1368, 1393, 1443, 1461, 1650, 1656, 1702, 2932, 2980, 3233, 3272; MS (ESI-TOF) $m/z$ 539.2 $[M + Na]^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{27}H_{36}N_2NaO_6S$ $[M + Na]^+$ 539.2182, found 539.2192.

*(E)-Methyl 6-((N-(tert-Butoxycarbonyl)sulfamoyl)amino)-5,5-diphenylhex-2-enoate (**2e**).* This compound was obtained according to the general procedure A. The subsequent chromatographic purification (hexanes/EtOAc, 3:1) gave 422 mg (0.89 mmol, 89%) of **2e** as a white solid: mp 144−146 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 7.63 (s, 1H), 7.57−7.06 (m, 10H), 6.56 (dt, $J$ = 15.6, 7.5 Hz, 1H), 5.88 (d, $J$ = 15.6 Hz, 1H), 4.56 (t, $J$ = 6.8 Hz, 1H), 3.69 (d, $J$ = 6.8 Hz, 2H), 3.67 (s, 3H), 3.14 (d, $J$ = 7.5 Hz, 2H), 1.40 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 166.2, 149.5, 143.5, 143.5, 128.5, 127.3, 127.0, 124.7, 83.7, 51.2, 50.2, 49.3, 39.3, 27.5; IR ($cm^{-1}$) 540, 578, 647, 698, 727, 822, 910, 1029, 1076, 1141, 1202, 1246, 1366, 1396, 1434, 1495, 1656, 1719, 2950, 2981, 3248; MS (ESI-TOF) $m/z$ 497.2 $[M + Na]^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{24}H_{30}N_2NaO_6S$ $[M + Na]^+$ 497.1719, found 497.1722.

*(E)-Methyl 6-((N-((Benzyloxy)carbonyl)sulfamoyl)amino)-5,5-diphenylhex-2-enoate (**2f**).* This compound was obtained according to the general procedure A. The subsequent chromatographic purification (hexanes/EtOAc, 4:1) gave 468 mg (0.92 mmol, 92%) of **2f** as a white solid: mp 147−153 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 7.72 (s, 1H), 7.33−7.09 (m, 15H), 6.55 (dt, $J$ = 15.6, 7.4 Hz, 1H), 5.85 (d, $J$ = 15.6 Hz, 1H), 5.12 (s, 2H), 4.63 (t, $J$ = 6.7 Hz, 1H), 3.68 (d, $J$ = 6.7 Hz, 2H), 3.65 (s, 3H), 3.09 (d, $J$ = 7.4 Hz, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 166.5, 150.9, 143.8, 143.6, 134.6, 128.8, 128.7, 128.7, 128.3, 127.5, 127.2, 124.8, 68.5, 51.4, 50.4, 49.6, 39.4; IR ($cm^{-1}$) 470, 550, 696, 745, 842, 1067, 1166, 1200, 1269, 1367, 1448, 1656, 1705, 3182, 3294; MS (ESI-TOF) $m/z$ 531.2 $[M + Na]^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{27}H_{28}N_2NaO_6S$ $[M + Na]^+$ 531.1581, found 531.1566.

*(E)-tert-Butyl 6-((N-(Methoxycarbonyl)sulfamoyl)amino)-5,5-diphenylhex-2-enoate (**2g**).* This compound was obtained according to the general procedure A. The subsequent chromatographic purification (hexanes/EtOAc, 3:1) gave 418 mg (0.88 mmol, 88%) of **2g** as a white solid: mp 75−79 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 7.34−7.10 (m, 11H), 6.43 (dt, $J$ = 15.6, 7.4 Hz, 1H), 5.76 (d, $J$ = 15.6 Hz, 1H), 4.64 (t, $J$ = 6.6 Hz, 1H), 3.70 (d, $J$ = 6.6 Hz, 2H), 3.65 (s, 3H), 3.07 (dd, $J$ = 7.4, 1.0 Hz, 2H), 1.41 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 165.6, 151.6, 143.7, 142.4, 128.6, 127.6, 127.1, 126.7, 80.3, 53.5, 50.4, 49.6, 39.4, 28.0; IR ($cm^{-1}$) 539, 583, 698, 730, 757, 772, 848, 961, 986, 1030, 1075, 1149, 1246, 1316, 1365, 1393, 1446, 1649, 1709, 1737, 2870, 2961, 3057, 3236; MS (ESI-TOF) $m/z$ 497.2 $[M + Na]^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{24}H_{30}N_2NaO_6S$ $[M + Na]^+$ 497.1719, found 497.1722.

*(E)-Methyl 6-((N-((Benzyloxy)carbonyl)sulfamoyl)amino)hex-2-enoate (**2h**).* This compound was obtained according to the general procedure A. The subsequent chromatographic purification (hexanes/EtOAc, 2:1) gave 418 mg (0.72 mmol, 72%) of **2h** as a white solid: mp 92−97 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 7.74 (s, 1H), 7.38−7.33 (m, 5H), 6.89 (dt, $J$ = 15.6, 6.9 Hz, 1H), 5.84 (d, $J$ = 15.6 Hz, 1H), 5.33 (t, $J$ = 6.2 Hz, 1H), 5.17 (s, 2H), 3.72 (s, 3H), 3.05 (dd, $J$ = 13.4, 6.9 Hz, 2H), 2.27−2.19 (m, 2H), 1.73−1.64 (m, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 166.9, 151.4, 147.3, 134.5, 128.9, 128.7, 128.5, 122.0, 68.6, 51.5, 43.1, 28.9, 27.5; IR ($cm^{-1}$) 696, 736, 776, 849, 977, 1153, 1243, 1343, 1433, 1657, 1720, 2954, 3262; MS (ESI-TOF) $m/z$ 379.1 $[M + Na]^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{15}H_{20}N_2NaO_6S$ $[M + Na]^+$ 379.0940, found 379.0945.

*(E)-tert-Butyl 4-(1-(((N-(Methoxycarbonyl)sulfamoyl)amino)-methyl)cyclohexyl)but-2-enoate (**2i**).* This compound was obtained according to the general procedure A. The subsequent chromatographic purification (hexanes/EtOAc, 4:1) gave 340 mg (0.87 mmol, 87%) of **2i** as a white solid: mp 86−96 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 8.20 (s, 1H), 6.81 (dt, $J$ = 15.6, 7.6 Hz, 1H), 5.80 (d, $J$ = 15.6 Hz, 1H), 5.38 (t, $J$ = 7.0 Hz, 1H), 3.78 (s, 3H), 2.91 (d, $J$ = 7.0 Hz, 2H), 2.20 (d, $J$ = 7.6 Hz, 2H), 1.46 (s, 9H), 1.45−1.31 (m, 10H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 165.8, 152.1, 143.2, 126.0, 80.4, 53.5, 49.7, 37.9, 36.9, 33.0, 28.1, 25.7, 21.2; IR ($cm^{-1}$) 587, 851, 1064, 1147, 1229, 1289, 1343, 1364, 1410, 1451, 1651, 1691, 1714, 1731, 1755, 2855, 2926, 3271; MS (ESI-TOF) $m/z$ 413.2 $[M + Na]^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{17}H_{30}N_2NaO_6S$ $[M + Na]^+$ 413.1741, found 413.1722.

*(E)-tert-Butyl 4-(1-(((N-(Isopropoxycarbonyl)sulfamoyl)amino)-methyl)cyclohexyl)but-2-enoate (**2j**).* This compound was obtained according to the general procedure A. The subsequent chromatographic purification (hexanes/EtOAc, 4:1) gave 343 mg (0.82 mmol, 82%) of **2j** as a white solid: mp 94−101 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 8.11 (s, 1H), 6.81 (dt, $J$ = 15.6, 7.6 Hz, 1H), 5.78 (d, $J$ = 15.6 Hz, 1H), 5.41 (t, $J$ = 6.9 Hz, 1H), 4.98 (hept, $J$ = 6.2 Hz, 1H), 2.90 (d, $J$ = 6.9 Hz, 2H), 2.19 (d, $J$ = 7.6 Hz, 2H), 1.45 (s, 9H), 1.44−1.30 (m, 10H), 1.26 (d, $J$ = 6.2 Hz, 6H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 165.7, 151.3, 143.2, 125.9, 80.20, 71.1, 49.7, 38.0, 36.9, 32.9, 28.1, 25.7, 21.7, 21.2; IR ($cm^{-1}$) 581, 748, 885, 1105, 1150, 1238, 1365, 1451, 1709, 2927, 3245; MS (ESI-TOF) $m/z$ 441.2 $[M + Na]^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{19}H_{34}N_2NaO_6S$ $[M + Na]^+$ 441.2046, found 441.2035.

*(E)-tert-Butyl 4-(1-(((N-(tert-Butoxycarbonyl)sulfamoyl)amino)-methyl)cyclohexyl)but-2-enoate (**2k**).* This compound was obtained according to the general procedure A. The subsequent chromatographic purification (hexanes/EtOAc, 4:1) gave 377 mg (0.87 mmol, 87%) of **2k** as a white solid: mp 121−126 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 7.74 (s, 1H), 6.81 (dt, $J$ = 15.6, 7.8 Hz, 1H), 5.78 (d, $J$ = 15.6 Hz, 1H), 5.27 (t, $J$ = 7.0 Hz, 1H), 2.88 (d, $J$ = 7.0 Hz, 2H), 2.19 (d, $J$ = 7.8 Hz, 2H), 1.47 (s, 9H), 1.45 (s, 9H), 1.44−1.30 (m, 10H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 165.6, 150.4, 143.1, 126.0, 83.6, 80.2, 49.7, 38.1, 36.9, 33.0, 28.1, 28.1, 25.7, 21.2; IR ($cm^{-1}$) 594, 724, 821, 950, 1136, 1254, 1368, 1442, 1691, 1712, 2927, 3232, 3302; MS (ESI-TOF) $m/z$ 455.2 $[M + Na]^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{20}H_{36}N_2NaO_6S$ $[M + Na]^+$ 455.2196, found 455.2192.

*(E)-Methyl 4-(1-(((N-(tert-Butoxycarbonyl)sulfamoyl)amino)-methyl)cyclohexyl)but-2-enoate (**2l**).* This compound was obtained according to the general procedure A. The subsequent chromatographic purification (hexanes/EtOAc, 3:1) gave 316 mg (0.81 mmol, 81%) of **2l** as a white solid: mp 127−131 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 7.75 (s, 1H), 6.91 (dt, $J$ = 15.6, 7.9 Hz, 1H), 5.88 (d, $J$ = 15.6 Hz, 1H), 5.33 (t, $J$ = 6.9 Hz, 1H), 3.69 (s, 3H), 2.88 (d, $J$ = 6.9 Hz, 2H), 2.23 (d, $J$ = 7.9 Hz, 2H), 1.46 (s, 9H), 1.45−1.30 (m, 10H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 166.6, 150.4, 144.7, 124.0, 83.7, 51.4, 49.6, 38.2, 36.9, 33.0, 27.9, 25.7, 21.2; IR ($cm^{-1}$) 570, 719, 818, 946, 1057, 1136, 1202, 1249, 1343, 1430, 1652, 1694, 1714, 2936, 3243, 3302; MS (ESI-TOF) $m/z$ 413.2 $[M + Na]^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{17}H_{30}N_2NaO_6S$ $[M + Na]^+$ 413.1741, found 413.1722.

*(E)-Methyl 6-((N-(tert-Butoxycarbonyl)sulfamoyl)amino)-5,5-dimethylhex-2-enoate (**2m**).* This compound was obtained according to the general procedure A. The subsequent chromatographic purification (hexanes/EtOAc, 3:1) gave 330 mg (0.94 mmol, 94%) of **2m** as a white solid: mp 126−129 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 7.64 (s, 1H), 6.96 (dt, $J$ = 15.6, 7,6 Hz,1H), 5.87 (d, $J$ = 15.6 Hz, 1H), 5.42−5.38 (m, 1H), 3.72 (s, 3H), 2.83 (d, $J$ = 6.8 Hz, 2H), 2.17 (d, $J$ = 7.6 Hz, 2H), 1.48 (s, 9H), 0.95 (s, 3H), 0.94 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 166.6, 150.3, 144.9, 124.0, 83.8, 53.5, 51.4,

42.0, 34.6, 27.9, 24.7; IR ($cm^{-1}$) 569, 582, 665, 670, 728, 820, 941, 1052, 1179, 1211, 1270, 1366, 1435, 1455, 1656, 1701, 1714, 1967, 3225, 3266; MS (ESI-TOF) $m/z$ 373.1 $[M + Na]^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{14}H_{26}N_2NaO_6S$ $[M + Na]^+$ 373.1396, found 373.1409.

*(E)-Ethyl 6-((N-(tert-Butoxycarbonyl)sulfamoyl)amino)-5,5-dimethylhex-2-enoate (**2n**).* This compound was obtained according to the general procedure A. The subsequent chromatographic purification (hexanes/EtOAc, 3:1) gave 299 mg (0.82 mmol, 82%) of **2n** as a white solid: mp 108−112 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ = 7.78 (s, 1H), 6.90 (dt, $J$ = 15.6, 7.8 Hz, 1H), 5.84 (d, $J$ = 15.6 Hz, 1H), 5.44 (t, $J$ = 6.9 Hz, 1H), 4.16 (q, $J$ = 7.1 Hz, 2H), 2.81 (d, $J$ = 6.9 Hz, 2H), 2.15 (d, $J$ = 7.8 Hz, 2H), 1.46 (s, 9H), 1.26 (t, $J$ = 7.1 Hz, 3H), 0.94 (s, 6H); $^{13}C$ NMR (101 MHz, $CDCl_3$) $\delta$ = 166.2, 150.4, 144.6, 124.3, 83.7, 60.2, 53.5, 42.0, 34.6, 27.9, 24.6, 14.2; IR ($cm^{-1}$) 581, 726, 818, 940, 979, 1049, 1136, 1254, 1346, 1365, 1444, 1656, 1698, 1720, 2969, 3231, 3289; MS (ESI-TOF) $m/z$ 387.2 $[M + Na]^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{15}H_{28}N_2NaO_6S$ $[M + Na]^+$ 387.1572, found 387.1566.

*(E)-Methyl 6-((N-(Isopropoxycarbonyl)sulfamoyl)amino)-5,5-dimethylhex-2-enoate (**2o**).* This compound was obtained according to the general procedure A. The subsequent chromatographic purification (hexanes/EtOAc, 3:1) gave 290 mg (0.86 mmol, 86%) of **2o** as a white solid: mp 113−116 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ = 7.96 (s, 1H), 6.97 (dt, $J$ = 15.6, 7.8 Hz, 1H), 5.90 (d, $J$ = 15.6 Hz, 1H), 5.55 (t, $J$ = 6.9 Hz, 1H), 5.09−4.98 (m, 1H), 3.76 (s, 3H), 2.88 (d, $J$ = 6.9 Hz, 2H), 2.21 (d, $J$ = 7.8 Hz, 2H), 1.32 (d, $J$ = 6.3 Hz, 6H), 0.99 (s, 6H); $^{13}C$ NMR (101 MHz, $CDCl_3$) $\delta$ = 166.7, 151.2, 144.9, 123.9, 71.3, 53.4, 51.5, 41.9, 34.7, 24.7, 21.7; IR ($cm^{-1}$) 583, 750, 790, 886, 950, 993, 1053, 1103, 1160, 1255, 1342, 1470, 1653, 1704, 1722, 2968, 3191, 3280; MS (ESI-TOF) $m/z$ 359.1 $[M + Na]^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{13}H_{24}N_2NaO_6S$ $[M + Na]^+$ 359.1272, found 359.1253.

**General Procedure for the Intramolecular Diamination of Acrylates (General Procedure B).** A Pyrex tube equipped with a stirrer bar was charged with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol, 0.1 equiv), $CuBr_2$ (223.4 mg, 1.0 mmol, 2 equiv), $Cs_2CO_3$ (488.7 mg, 1.5 mmol, 3 equiv), and sulfamide (0.5 mmol, 1.0 equiv). DMF (4 mL) was added, and the mixture was stirred for 12 h at 40 °C. The reaction was quenched by addition of 2 mL of satd aqueous $Na_2S_2O_3$ solution. The aqueous phase was extracted with ethyl acetate (3×), the combined organic layers were dried ($MgSO_4$), and the solvent was evaporated under reduced pressure. The crude reaction mixture was then analyzed by NMR and the conversion of alkene was 90−100%. All products were purified by flash chromatography (hexanes/EtOAc).

*anti-Dimethyl 5,5-Diphenyltetrahydropyrrolo[1,2-b][1,2,5]-thiadiazole-2,3(3H)-dicarboxylate 1,1-Dioxide (**3a**).* This compound was obtained according to the general procedure B. The subsequent chromatographic purification (hexanes/EtOAc, 3:1) gave 140 mg (0.33 mmol, 65%) of **3a** as a white solid: mp 200−205 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ = 7.40−7.25 (m, 10H), 4.51 (d, $J$ = 3.6 Hz, 1H), 4.24 (d, $J$ = 10.4 Hz, 1H), 4.14 (ddd, $J$ = 7.3, 6.6, 3.6 Hz, 1H), 4.08 (d, $J$ = 10.4 Hz, 1H), 3.91 (s, 3H), 3.82 (s, 3H), 3.19 (dd, $J$ = 12.9, 6.6 Hz, 1H), 2.74 (dd, $J$ = 12.9, 7.3 Hz, 1H); $^{13}C$ NMR (101 MHz, $CDCl_3$) $\delta$ = 168.1, 150.9, 143.9, 143.7, 128.8, 128.7, 127.0, 126.5, 125.4, 61.9, 60.0, 59.0, 55.0, 53.5, 46.3; IR ($cm^{-1}$) 583, 708, 801, 906, 983, 1023, 1085, 1112, 1140, 1166, 1178, 1207, 1249, 1271, 1307, 1371, 1432, 1736, 1753, 2897, 2957; MS (ESI-TOF) $m/z$ 453.1 $[M + Na]^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{21}H_{22}N_2NaO_6S$ $[M + Na]^+$ 453.1096, found 453.1088.

*syn-Dimethyl 5,5-Diphenyltetrahydropyrrolo[1,2-b][1,2,5]-thiadiazole-2,3(3H)-dicarboxylate 1,1-Dioxide (**4a**).* This compound was obtained according to the general procedure B. The subsequent chromatographic purification (hexanes/EtOAc, 3:1) gave 63 mg (0.15 mmol, 29%) of **4a** as a white solid: mp 197−200 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ = 7.36−7.09 (m, 10H), 4.76 (d, $J$ = 8.7 Hz, 1H), 4.36 (ddd, $J$ = 8.7, 8.7, 6.7 Hz, 1H), 4.25 (dd, $J$ = 9.6, 1.3 Hz, 1H), 3.93 (d, $J$ = 9.6 Hz, 1H), 3.91 (s, 3H), 3.73 (s, 3H), 2.78 (ddd, $J$ = 12.9, 6.7, 1.3 Hz, 1H), 2.43 (dd, $J$ = 12.9, 8.7 Hz, 1H); $^{13}C$ NMR (101 MHz, $CDCl_3$) $\delta$ = 167.5, 151.4, 143.8, 143.7, 128.5, 128.5, 127.0, 126.8, 126.2, 126.2, 60.0, 59.1, 56.7, 55.2, 54.6, 52.7, 40.1; IR ($cm^{-1}$) 520, 560, 595, 631, 676, 698, 723, 758, 822, 900, 961, 982, 1017, 1087, 1116, 1174, 1308, 1363, 1437, 1493, 1737, 2951; MS (ESI-TOF) $m/z$ 453.1 $[M + Na]^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{21}H_{22}N_2NaO_6S$ $[M + Na]^+$ 453.1096, found 453.1088.

*Methyl 2-Bromo-2-(1-(N-(methoxycarbonyl)sulfamoyl)-4,4-diphenylpyrrolidin-2-yl)acetate (**5**).* This compound was obtained according to the general procedure B, but the temperature was changed to rt. The subsequent chromatographic purification (hexanes/EtOAc, 3:1) gave 82 mg (0.16 mmol, 32%) of **5** as a white solid: mp 166−176 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ = 7.44−7.17 (m, 11H), 5.27 (d, $J$ = 3.4 Hz, 1H), 4.64 (m, 2H), 4.09 (d, $J$ = 11.1 Hz, 1H), 3.79 (s, 3H), 3.54 (s, 3H), 3.33 (dd, $J$ = 13.3, 7.8 Hz, 1H), 2.83 (dd, $J$ = 13.3, 9.4 Hz, 1H); $^{13}C$ NMR (101 MHz, $CDCl_3$) $\delta$ = 168.3, 151.3, 144.6, 143.30, 128.8, 128.7, 126.8, 126.7, 126.6, 126.4, 60.5, 59.8, 53.3, 53.2, 52.8, 50.8, 40.0; IR ($cm^{-1}$) 570, 608, 697, 705, 772, 841, 998, 1057, 1079, 1144, 1156, 1164, 1209, 1231, 1279, 1307, 1356, 1367, 1429, 1469, 1729, 3232, 3303; MS (ESI-TOF) $m/z$ 533.0 $[M + Na]^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{21}H_{23}BrN_2NaO_6S$ $[M + Na]^+$ 533.0358, found 533.0361.

*anti-2-Benzyl 3-tert-Butyl 5,5-Diphenyltetrahydropyrrolo[1,2-b][1,2,5]thiadiazole-2,3(3H)-dicarboxylate 1,1-Dioxide (**3b**).* This compound was obtained according to the general procedure B. The subsequent chromatographic purification (hexanes/EtOAc 3:1) gave 214 mg (0.39 mmol, 78%) of **3b** as a white solid: mp 84−89 °C; $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ = 7.46−7.21 (m, 15H), 5.32 (d, $J$ = 12.3 Hz, 1H), 5.28 (d, $J$ = 12.3 Hz, 1H), 4.32 (d, $J$ = 4.0 Hz, 1H), 4.21 (d, $J$ = 10.4 Hz, 1H), 4.15−4.10 (m, 1H), 4.09 (d, $J$ = 10.4 Hz, 1H), 3.16 (dd, $J$ = 12.7, 6.7 Hz, 1H), 2.71 (dd, $J$ = 12.7, 7.2 Hz, 1H), 1.41 (s, 9H); $^{13}C$ NMR (126 MHz, $CDCl_3$) $\delta$ = 166.9, 150.4, 144.2, 143.9, 134.8, 128.8, 128.7, 128.6, 128.5, 128.2, 127.2, 127.0, 126.5, 126.5, 83.9, 68.9, 62.6, 60.1, 59.2, 55.0, 44.9, 27.7; IR ($cm^{-1}$) 537, 582, 626, 696, 749, 801, 844, 1026, 1093, 1150, 1293, 1369, 1448, 1495, 1729, 2930, 2976; MS (ESI-TOF) $m/z$ 571.2 $[M + Na]^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{30}H_{32}N_2NaO_6S$ $[M + Na]^+$ 571.1879, found 571.1865.

*anti-2-Benzyl 3-Ethyl 5,5-Diphenyltetrahydropyrrolo[1,2-b][1,2,5]thiadiazole-2,3(3H)-dicarboxylate 1,1-Dioxide (**3c**).* This compound was obtained according to the general procedure B. The subsequent chromatographic purification (hexanes/EtOAc 3:1) gave 177 mg (0.34 mmol, 68%) of **3c** as a white solid: $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ = 7.44−7.18 (m, 15H), 5.32 (d, $J$ = 12.7 Hz, 1H), 5.25 (d, $J$ = 12.7 Hz, 1H), 4.41 (d, $J$ = 4.6 Hz, 1H), 4.22−4.18 (m, 2H), 4.16−4.10 (m, 2H), 4.10−4.06 (m, 1H), 3.15 (dd, $J$ = 12.8, 6.7 Hz, 1H), 2.71 (dd, $J$ = 12.8, 7.2 Hz, 1H), 1.18 (t, $J$ = 7.1 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) $\delta$ = 167.7, 150.3, 144.0, 143.7, 134.7, 128.8, 128.7, 128.5, 128.4, 128.0, 127.2, 126.9, 126.5, 126.4, 69.0, 62.5, 62.0, 59.9, 59.0, 55.0, 44.8, 13.9; IR ($cm^{-1}$) 539, 584, 626, 695, 750, 857, 968, 1020, 1093, 1178, 1296, 1371, 1448, 1496, 1598, 1732, 2925, 2961; MS (ESI-TOF) $m/z$ 543.1$[M + Na]^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{28}H_{28}N_2NaO_6S$ $[M + Na]^+$ 543.1566, found 543.1597.

*anti-Di-tert-butyl 5,5-Diphenyltetrahydropyrrolo[1,2-b][1,2,5]-thiadiazole-2,3(3H)-dicarboxylate 1,1-Dioxide (**3d**).* This compound was obtained according to the general procedure B. The subsequent chromatographic purification on HPLC (hexanes/isopropanol 98:2) gave 147 mg (0.29 mmol, 57%) of **3d** as a white solid: mp 175−178 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ = 7.34−7.18 (m, 10H), 4.23 (brs, 1H), 4.17 (d, $J$ = 10.4 Hz, 1H), 4.07 (d, $J$ = 10.4 Hz, 1H), 4.05−4.00 (m, 1H), 3.13 (dd, $J$ = 12.7, 6.7 Hz, 1H), 2.69 (dd, $J$ = 12.7, 7.1 Hz, 1H), 1.52 (s, 9H), 1.47 (s, 9H); $^{13}C$ NMR (101 MHz, $CDCl_3$) $\delta$ = 167.1, 148.8, 144.0, 143.9, 128.5, 128.5, 126.9, 126.7, 126.3, 126.3, 84.3, 83.3, 62.3, 59.8, 58.6, 54.7, 44.6, 27.7, 27.6; IR ($cm^{-1}$) 627, 699, 752, 841, 1028, 1070, 1093, 1147, 1180, 1218, 1258, 1304, 1333, 1368, 1449, 1477, 1726, 2935, 2980; MS (ESI-TOF) $m/z$ 537.2 $[M + Na]^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{27}H_{34}N_2NaO_6S$ $[M + Na]^+$ 537.2035, found 537.2014.

*syn-Di-tert-butyl 5,5-Diphenyltetrahydropyrrolo[1,2-b][1,2,5]-thiadiazole-2,3(3H)-dicarboxylate 1,1-Dioxide (**4d**).* This compound was obtained according to the general procedure. The subsequent chromatographic purification on HPLC (hexanes/isopropanol 98:2)


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gave 57 mg (0.11 mmol, 22%) of **3d** as a white solid: mp 99−103 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ = 7.36−7.13 (m, 10H), 4.56 (d, $J$ = 8.5 Hz, 1H), 4.35 (m, 1H), 4.22 (dd, $J$ = 9.4, 1.0 Hz, 1H), 3.95 (d, $J$ = 9.4 Hz, 1H), 2.84 (ddd, $J$ = 12.7, 7.0, 1.0 Hz, 1H), 2.55 (dd, $J$ = 12.7, 9.0 Hz, 1H), 1.57 (s, 9H), 1.42 (s, 9H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ = 166.8, 149.7, 144.5, 144.2, 128.7, 128.7, 127.1, 127.0, 126.6, 126.5, 85.1, 83.8, 61.1, 59.0, 56.7, 55.6, 39.9, 27.9, 27.8; IR (cm$^{-1}$) 591, 633, 700, 759, 841, 866, 1028, 1043, 1075, 1146, 1229, 1258, 1333, 1368, 1730, 2935, 2981; MS (ESI-TOF) $m/z$ 537.2 [M + Na]$^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{27}H_{34}N_2NaO_6S$ [M + Na]$^+$ 537.2035, found 537.2014.

*anti-2-tert-Butyl 3-Methyl 5,5-Diphenyltetrahydropyrrolo[1,2-b][1,2,5]thiadiazole-2,3(3H)-dicarboxylate 1,1-Dioxide (**3e**).* This compound was obtained according to the general procedure B. The subsequent chromatographic purification (hexanes/EtOAc 3:1) gave 170 mg (0.36 mmol, 72%) of **3e** as a white solid: mp 85−96 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ = 7.35−7.19 (m, 10H), 4.38 (m, 1H), 4.18 (dd, $J$ = 10.4, 0.9 Hz, 1H), 4.11−4.01 (m, 2H), 3.78 (s, 3H), 3.13 (ddd, $J$ = 12.7, 6.6, 0.9 Hz, 1H), 2.71 (dd, $J$ = 12.7, 7.4 Hz, 1H), 1.52 (s, 9H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ = 168.6, 149.1, 144.1, 144.0, 128.8, 128.7, 127.2, 127.0, 126.6, 126.5, 85.0, 61.9, 59.9, 58.7, 55.0, 53.1, 44.8, 27.9; IR (cm$^{-1}$) 632, 701, 751, 832, 976, 1057, 1091, 1134, 1148, 1175, 1193, 1212, 1255, 1312, 1337, 1349, 1368, 1448, 1712, 1737, 1750, 2948, 2987; MS (ESI-TOF) $m/z$ 495.2 [M + Na]$^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{24}H_{28}N_2NaO_6S$ [M + Na]$^+$ 495.1566, found 495.1569.

*anti-2-Benzyl 3-Methyl 5,5-Diphenyltetrahydropyrrolo[1,2-b][1,2,5]thiadiazole-2,3(3H)-dicarboxylate 1,1-Dioxide (**3f**).* This compound was obtained according to the general procedure B. The subsequent chromatographic purification (hexanes/EtOAc 3:1) gave 212 mg (0.42 mmol, 84%) of **3f** as a white solid: mp 115−117 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 7.43−7.20 (m, 15H), 5.40−5.23 (m, 2H), 4.42 (d, $J$ = 4.6 Hz, 1H), 4.18 (d, $J$ = 10.4 Hz, 1H), 4.13−4.05 (m, 2H), 3.69 (s, 3H), 3.14 (dd, $J$ = 12.7, 6.7 Hz, 1H), 2.70 (dd, $J$ = 12.7, 7.2 Hz, 1H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 168.2, 150.3, 144.0, 143.7, 134.7, 128.8, 128.7, 128.6, 128.5, 128.0, 127.3, 127.0, 126.5, 126.4, 69.1, 61.9, 59.9, 59.0, 55.0, 53.2, 44.8; IR (cm$^{-1}$) 542, 591, 626, 748, 968, 990, 1026, 1044, 1072, 1093, 1175, 1211, 1299, 1370, 1447, 1495, 1733, 2925, 2954, 3030; MS (ESI-TOF) $m/z$ 529.1 [M + Na]$^+$ (100); HRMS-ESI-TOF $m/z$ calculated for $C_{27}H_{26}N_2NaO_6S$ [M + Na]$^+$ 529.1409, found 529.1410.

*anti-3-tert-Butyl 2-Methyl 5,5-Diphenyltetrahydropyrrolo[1,2-b][1,2,5]thiadiazole-2,3(3H)-dicarboxylate 1,1-Dioxide (**3g**).* This compound was obtained according to the general procedure B. The subsequent chromatographic purification (hexanes/EtOAc 3:1) gave 180 mg (0.38 mmol, 76%) of **3g** as a white solid: mp 128−131 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 7.36−7.22 (m, 10H), 4.36 (d, $J$ = 4.4 Hz, 1H), 4.23 (dd, $J$ = 10.3, 1.1 Hz, 1H), 4.12 (m, 1H), 4.03 (d, $J$ = 10.3 Hz, 1H), 3.89 (s, 3H), 3.15 (ddd, $J$ = 12.8, 6.7, 1.1 Hz, 1H), 2.69 (dd, $J$ = 12.8, 7.4 Hz, 1H), 1.48 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 166.8, 151.1, 144.1, 144.0, 128.8, 128.7, 127.2, 127.0, 126.5, 126.5, 83.9, 62.7, 60.1, 59.2, 55.0, 54.3, 44.8, 27.8; IR (cm$^{-1}$) 632, 700, 760, 812, 909, 1092, 1111, 1131, 1151, 1183, 1226, 1260, 1305, 1360, 1370, 1443, 1739, 1754, 2975; MS (ESI-TOF) $m/z$ 495.2 [M + Na]$^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{24}H_{28}N_2NaO_6S$ [M + Na]$^+$ 495.1566, found 495.1583.

*anti-2-Benzyl 3-Methyl Tetrahydropyrrolo[1,2-b][1,2,5]thiadiazole-2,3(3H)-dicarboxylate 1,1-Dioxide (**3h**).* This compound was obtained according to the general procedure B. The subsequent chromatographic purification (hexanes/EtOAc 3:1) gave 124 mg (0.35 mmol, 70%) of **3h** as a colorless wax: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ = 7.43−7.30 (m, 5H), 5.35 (d, $J$ = 12.4 Hz, 1H), 5.25 (d, $J$ = 12.4 Hz, 1H), 4.30 (d, $J$ = 7.1 Hz, 1H), 4.05 (dt, $J$ = 7.1, 2.2 Hz, 1H), 3.77−3.66 (m, 4H), 3.42 (dt, $J$ = 11.2, 7.6 Hz, 1H), 2.37−2.29 (m, 1H), 2.17−2.10 (m, 1H), 2.05−1.99 (m, 2H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ = 168.2, 150.4, 134.7, 128.6, 128.5, 127.9, 69.1, 62.9, 60.2, 53.1, 51.0, 31.2, 23.2; IR (cm$^{-1}$) 652, 697, 735, 788, 909, 976, 1074, 1171, 1300, 1368, 1438, 1454, 1498, 1502, 1729, 2956, 3034; MS (ESI-TOF) $m/z$ 377.1 [M + Na]$^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{15}H_{18}N_2NaO_6S$ [M + Na]$^+$ 377.0783, found 377.0791.

*anti-3′-tert-Butyl 2′-Methyl Dihydro-2′H-spiro[cyclohexane-1,5′-pyrrolo[1,2-b][1,2,5]thiadiazole]-2′,3′(3′H,6′H)-dicarboxylate 1′,1′-Dioxide (**3i**).* This compound was obtained according to the general procedure B. The subsequent chromatographic purification (hexanes/EtOAc 3:1) gave 156 mg (0.40 mmol, 80%) of **3i** as a white solid: mp 176−178 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ = 4.32 (d, $J$ = 6.4 Hz, 1H), 4.01 (ddd, $J$ = 7.7, 6.4, 5.0 Hz, 1H), 3.88 (s, 3H), 3.34 (d, $J$ = 10.1 Hz, 1H), 3.14 (d, $J$ = 10.1 Hz, 1H), 2.28 (dd, $J$ = 13.4, 7.7 Hz, 1H), 1.78 (dd, $J$ = 13.4, 5.0 Hz, 1H), 1.55−1.39 (m, 19H). $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ = 166.9, 151.2, 83.6, 64.3, 59.5, 54.2, 43.9, 36.9, 35.9, 27.8, 25.6, 23.8, 22.9; IR (cm$^{-1}$) 578, 611, 969, 1080, 1150, 1185, 1220, 1250, 1267, 1330, 1350, 1367, 1436, 1726, 1755, 2859, 2926; MS (ESI-TOF) $m/z$ 411.2 [M + Na]$^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{17}H_{28}N_2NaO_6S$ [M + Na]$^+$ 411.1566, found 411.1559.

*anti-3′-tert-Butyl 2′-Isopropyl Dihydro-2′H-spiro[cyclohexane-1,5′-pyrrolo[1,2-b][1,2,5]thiadiazole]-2′,3′(3′H,6′H)-dicarboxylate 1′,1′-Dioxide (**3j**).* This compound was obtained according to the general procedure B. The subsequent chromatographic purification (hexanes/EtOAc 3:1) gave 156 mg (0.37 mmol, 75%) of **3j** as a white solid: mp 128−131 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ = 5.08 (dq, $J$ = 6.3, 6.3 Hz, 1H), 4.33 (d, $J$ = 6.4 Hz, 1H), 4.01 (m, 1H), 3.37 (d, $J$ = 10.0 Hz, 1H), 3.16 (d, $J$ = 10.0 Hz, 1H), 2.30 (dd, $J$ = 13.3, 7.7 Hz, 1H), 1.81 (dd, $J$ = 13.3, 5.1 Hz, 1H), 1.58−1.42 (m, 10H), 1.51 (s, 9H), 1.38 (d, $J$ = 6.3 Hz, 3H), 1.36 (d, $J$ = 6.3 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 167.1, 150.4, 83.4, 72.2, 64.1, 59.5, 43.9, 37.0, 36.0, 27.9, 25.6, 23.9, 22.9, 21.9, 21.6; IR (cm$^{-1}$) 549, 579, 613, 654, 681, 819, 877, 909, 950, 977, 1001, 1073, 1146, 1248, 1319, 1378, 1448, 1719, 1755, 2853, 2937, 2982; MS (ESI-TOF) $m/z$ 439.2 [M + Na]$^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{19}H_{32}N_2NaO_6S$ [M + Na]$^+$ 439.1879, found 439.1889.

*anti-Di-tert-butyl Dihydro-2′H-Spiro[cyclohexane-1,5′-pyrrolo-[1,2-b][1,2,5]thiadiazole]-2′,3′(3′H,6′H)-dicarboxylate 1′,1′-Dioxide (**3k**).* This compound was obtained according to the general procedure B. The subsequent chromatographic purification (hexanes/EtOAc 3:1) gave 151 mg (0.35 mmol, 70%) of **3k** as a white solid: mp 139−141 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ = 4.25 (d, $J$ = 6.3 Hz, 1H), 3.96 (m, 1H), 3.32 (d, $J$ = 10.0 Hz, 1H), 3.14 (d, $J$ = 10.0 Hz, 1H), 2.26 (dd, $J$ = 13.3, 7.8 Hz, 1H), 1.77 (dd, $J$ = 13.3, 5.1 Hz, 1H), 1.54 (s, 9H), 1.62−1.39 (m, 10H), 1.48 (s, 9H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ = 167.3, 149.4, 84.5, 83.3, 64.1, 59.3, 43.9, 37.0, 36.0, 28.0, 27.9, 25.6, 23.9, 22.9; IR (cm$^{-1}$) 539, 594, 627, 769, 816, 924, 983, 1010, 1073, 1153, 1187, 1220, 1267, 1315, 1365, 1451, 1716, 1756, 2852, 2928, 2978; MS (ESI-TOF) $m/z$ 453.2 [M + Na]$^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{20}H_{34}N_2NaO_6S$ [M + Na]$^+$ 453.2035, found 453.2038.

*anti-2′-tert-Butyl 3′-Methyl Dihydro-2′H-spiro[cyclohexane-1,5′-pyrrolo[1,2-b][1,2,5]thiadiazole]-2′,3′(3′H,6′H)-dicarboxylate 1′,1′-Dioxide (**3l**).* This compound was obtained according to the general procedure B. The subsequent chromatographic purification (hexanes/EtOAc 3:1) gave 136 mg (0.35 mmol, 70%) of **3l** as a white solid: mp 92−95 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ = 4.39 (d, $J$ = 6.5 Hz, 1H), 4.02 (ddd, $J$ = 7.7, 6.5, 5.0 Hz, 1H), 3.80 (s, 3H), 3.34 (d, $J$ = 10.0 Hz, 1H), 3.15 (d, $J$ = 10.0 Hz, 1H), 2.27 (dd, $J$ = 13.4, 7.7 Hz, 1H), 1.78 (dd, $J$ = 13.4, 5.0 Hz, 1H), 1.58−1.38 (m, 19H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 168.6, 149.2, 84.8, 63.5, 59.1, 52.9, 43.9, 43.1, 36.9, 35.9, 27.9, 27.8, 25.5, 23.8, 22.9; IR (cm$^{-1}$) 584, 596, 609, 624, 724, 853, 912, 976, 1072, 1099, 1143, 1165, 1183, 1207, 1258, 1331, 1358, 1450, 1721, 1753, 2853, 2931; MS (ESI-TOF) $m/z$ 411.2 [M + Na]$^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{17}H_{28}N_2NaO_6S$ [M + Na]$^+$ 411.1566, found 411.1566.

*anti-2-tert-Butyl 3-Methyl 5,5-Dimethyltetrahydropyrrolo[1,2-b][1,2,5]thiadiazole-2,3(3H)-dicarboxylate 1,1-Dioxide (**3m**).* This compound was obtained according to the general procedure B. The subsequent chromatographic purification (hexanes/EtOAc 3:1) gave 127 mg (0.36 mmol, 73%) of **3m** as a colorless wax: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ = 4.41 (d, $J$ = 6.3 Hz, 1H), 4.06 (m, 1H), 3.79 (s, 3H), 3.21 (d, $J$ = 9.7 Hz, 1H), 3.15 (d, $J$ = 9.7 Hz, 1H), 2.20 (dd, $J$ = 13.1, 7.6 Hz, 1H), 1.81 (dd, $J$ = 13.1, 5.9 Hz, 1H), 1.52 (s, 9H), 1.20 (s, 3H), 1.16 (s, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ = 168.6, 149.2, 84.8, 63.4, 62.5, 59.4, 52.9, 45.9, 40.0, 27.8, 27.4, 26.5; IR (cm$^{-1}$) 462, 515, 568, 625, 696, 752, 815, 880, 962, 988, 1035, 1080, 1143, 1172,

1257, 1307, 1366, 1458, 1726, 2875, 2961; MS (ESI-TOF) $m/z$ 371.1 $[M + Na]^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{14}H_{24}N_2NaO_6S$ $[M + Na]^+$ 371.1253, found 371.1237.

*anti-2-tert-Butyl 3-Ethyl 5,5-Dimethyltetrahydropyrrolo[1,2-b][1,2,5]thiadiazole-2,3(3H)-dicarboxylate 1,1-dioxide (**3n**).* This compound was obtained according to the general procedure B. The subsequent chromatographic purification (hexanes/EtOAc 3:1) gave 118 mg (0.32 mmol, 65%) of **3n** as a white solid: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 4.41 (d, $J$ = 6.1 Hz, 1H), 4.31−4.22 (m, 2H), 4.07 (m, 1H), 3.22 (d, $J$ = 9.7 Hz, 1H), 3.16 (dd, $J$ = 9.7, 0.6 Hz, 1H), 2.22 (ddd, $J$ = 13.1, 7.5, 0.6 Hz, 1H), 1.83 (dd, $J$ = 13.1, 5.9 Hz, 1H), 1.54 (s, 9H), 1.30 (t, $J$ = 7.1 Hz, 3H), 1.21 (s, 3H), 1.17 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 168.1, 149.3, 84.7, 63.4, 62.6, 62.2, 59.5, 46.0, 40.0, 27.9, 27.4, 26.5, 14.0; IR ($cm^{-1}$) 569, 624, 1034, 1080, 1143, 1176, 1257, 1308, 1368, 1727, 2937, 2968; MS (ESI-TOF) $m/z$ 385.1 $[M + Na]^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{15}H_{26}N_2NaO_6S$ $[M + Na]^+$ 385.1409, found 385.1409.

*anti-2-Isopropyl 3-Methyl 5,5-Dimethyltetrahydropyrrolo[1,2-b][1,2,5]thiadiazole-2,3(3H)-dicarboxylate 1,1-Dioxide (**3o**).* This compound was obtained according to the general procedure B. The subsequent chromatographic purification (hexanes/EtOAc 3:1) gave 125 mg (0.37 mmol, 75%) of **3o** as a white solid: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 5.04 (dq, $J$ = 6.4, 6.4 Hz, 1H), 4.46 (d, $J$ = 6.2 Hz, 1H), 4.09 (m, 1H), 3.80 (s, 3H), 3.21(d, $J$ = 9.7 Hz, 1H), 3.17(d, $J$ = 9.7 Hz, 1H), 2.23 (dd, $J$ = 13.0, 7.5 Hz, 1H), 1.82 (dd, $J$ = 13.0, 5.8 Hz, 1H), 1.35 (d, $J$ = 6.4 Hz, 3H), 133 (d, $J$ = 6.4 Hz, 3H), 1.20 (s, 3H), 1.17 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 168.5, 150.2, 72.5, 63.5, 62.6, 59.6, 53.1, 46.1, 40.1, 27.4, 26.5, 21.7, 21.6; IR ($cm^{-1}$) 567, 625, 766, 906, 963, 987, 1038, 1080, 1098, 1171, 1292, 1362, 1438, 1465, 1729, 2875, 2961; MS (ESI-TOF) $m/z$ 357.1 $[M + Na]^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{13}H_{22}N_2O_6SNa$ $[M + Na]^+$ 357.1096, found 357.1093.

*anti-5,5-Diphenylhexahydropyrrolo[1,2-b][1,2,5]thiadiazole-3-carboxylic Acid 1,1-Dioxide (**6**).* An aqueous solution of KOH (5N, 20 mL) was added to a solution of sulfamide (1.00 mmol) in 10 mL of THF/MeOH (5:1) at rt. After 2 h at 40 °C, the resulting solution was cooled to 0 °C and adjusted to pH ∼2 by dropwise addition of aqueous HCl solution (12 N). The reaction mixture was extracted with $CHCl_3$ (3×), and the combined organic layers were dried ($MgSO_4$). The solvent was removed under reduced pressure, and the crude product was purified by crystallization from $CH_2Cl_2$/MeOH/hexanes to give 301 mg (0.84 mmol, 84%) of the deprotected product **6** as a white solid: mp 74−75 °C; $^1$H NMR (500 MHz, acetone-$d_6$) $\delta$ = 7.53−7.45 (m, 2H), 7.38−7.31 (m, 6H), 7.27−7.20 (m, 2H), 6.69 (d, $J$ = 5.9 Hz, 1H), 4.45−4.38 (m, 1H), 4.35−4.29 (m, 2H), 3.71 (d, $J$ = 9.6 Hz, 1H), 3.18 (dd, $J$ = 12.5, 6.2 Hz, 1H), 2.62 (dd, $J$ = 12.5, 9.9 Hz, 1H); $^{13}$C NMR (126 MHz, acetone-$d_6$) $\delta$ = 171.1, 147.1, 146.2, 130.1, 130.0, 128.3, 128.2, 128.1, 128.1, 67.9, 62.2, 59.2, 58.9, 44.5; IR ($cm^{-1}$) 509, 588, 621, 696, 752, 774, 809, 869, 907, 966, 1026, 1103, 1164, 1268, 1323, 1447, 1494, 1598, 1732, 2598, 2873, 2926, 2957, 3026, 3058; MS (ESI-TOF) $m/z$ 357.1 $[M - H]^-$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{18}H_{17}N_2O_4S$ $[M - H]^-$ 357.0909, found 357.0909.

*Methyl 2-(anti-1,1-Dioxido-5,5-diphenylhexahydropyrrolo[1,2-b][1,2,5]thiadiazole-3-carboxamido)acetate (**7**).* A solution of glycine methyl ester hydrochloride (100 mg, 0.80 mmol) and sulfamide **6** (287 mg, 0.80 mmol) in $CH_2Cl_2$ (4 mL) was treated with DIEA (140 μL, 0.80 mmol), EDCl (154 mg, 0.80 mmol), and HOBt (108 mg, 0.8 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 1 h and then at 25 °C for 17 h. The reaction mixture was washed with water (3 mL), 2 N HCl (3 mL), saturated $NaHCO_3$ solution (5 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure and the crude product was purified by chromatography on silica gel ($CHCl_3$/MeOH 95:5) to give 178 mg (0.42 mmol, 52%) of **7** as a white solid: mp 208−210 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ = 7.35−7.15 (m, 10H), 6.97 (t, $J$ = 5.4 Hz, 1H), 4.42 (d, $J$ = 8.2 Hz, 1H), 4.27 (m, 2H), 4.11 (dd, $J$ = 18.0, 5.4 Hz, 1H), 4.04 (dd, $J$ = 18.0, 5.4 Hz, 1H), 3.74 (s, 3H), 3.73−3.69 (m, 2H), 2.55 (dd, $J$ = 12.2, 5.6 Hz, 1H), 2.48 (dd, $J$ = 11.4, 12.2 Hz, 1H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ = 169.6, 167.4, 144.5, 143.7, 128.6, 128.6, 127.0, 126.8, 126.8, 126.5, 64.2, 59.1, 56.6, 56.1, 52.5, 41.0, 39.3; IR ($cm^{-1}$) 514, 589, 700, 752, 786, 863, 908, 1026, 1163, 1225, 1337, 1352, 1406, 1437, 1447, 1489, 1550, 1653, 1745, 2909, 2957, 3029, 3133, 3354; MS (ESI-TOF) $m/z$ 452.1 $[M + Na]^+$ (100); HRMS-ESI-TOF $m/z$ calcd for $C_{21}H_{23}N_3NaO_5S$ $[M + Na]^+$ 452.1256, found 452.1240.

## ■ ASSOCIATED CONTENT

### Ⓢ Supporting Information

$^1$H and $^{13}$C spectra for the new compounds; graphics of the crystal structures showing thermal ellipsoids with 50% probability. This material is available free of charge via the Internet at http://pubs.acs.org.

## ■ AUTHOR INFORMATION

### Corresponding Author

*E-mail: kmuniz@iciq.es.

### Notes

The authors declare no competing financial interest.

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## ■ REFERENCES

(1) Wang, L.; Schultz, P. J. *Angew. Chem., Int. Ed* **2004**, *44*, 34.

(2) Viso, A.; Fernández de la Pradilla, R.; Tortosa, M.; García, A.; Flores, A. *Chem. Rev.* **2011**, *111*, PR1.

(3) Gómez Arrayas, R.; Carretero, J. C. *Chem. Soc. Rev.* **2009**, *38*, 1940.

(4) Cardona, F.; Goti, A. *Nature Chem.* **2009**, *1*, 269. de Figueiredo, R. M. *Angew. Chem., Int. Ed.* **2009**, *48*, 1190. Muñiz, K.; Hövelmann, C. H.; Streuff, J.; Campos-Gómez, E. *Pure Appl. Chem.* **2008**, *80*, 1089.

(5) (a) Streuff, J.; Hövelmann, C. H.; Nieger, M.; Muñiz, K. *J. Am. Chem. Soc.* **2005**, *127*, 14586. (b) Muñiz, K.; Hövelmann, C. H.; Streuff, J. *J. Am. Chem. Soc.* **2008**, *130*, 763. (c) Muñiz, K. *J. Am. Chem. Soc.* **2007**, *129*, 14542. (d) Hövelmann, C. H.; Streuff, J.; Brelot, L.; Muñiz, K. *Chem. Commun.* **2008**, 2334. (e) Muñiz, K.; Hövelmann, C. H.; Campos-Gómez, E.; Barluenga, J.; González, J. M.; Streuff, J.; Nieger, M. *Chem. Asian J.* **2008**, *3*, 776. (f) Sibbald, P. A.; Michael, F. E. *Org. Lett.* **2009**, *11*, 1147. (g) Sibbald, P. A.; Rosewall, C. F.; Swartz, R. D.; Michael, F. E. *J. Am. Chem. Soc.* **2009**, *131*, 15945. (h) Iglesias, A.; Pérez, E. G.; Muñiz, K. *Angew. Chem., Int. Ed.* **2010**, *49*, 8109. (i) Muñiz, K.; Kirsch, J.; Chávez, P. *Adv. Synth. Catal.* **2011**, *353*, 689.

(6) Muñiz, K.; Streuff, J.; Hövelmann, C. H.; Nuñez, A. *Angew. Chem., Int. Ed.* **2007**, *469*, 7125.

(7) Iglesias, A.; Muñiz, K. *Chem.—Eur. J.* **2009**, *15*, 10563.

(8) (a) Sequeira, F. C.; Turnpenny, B. W.; Chemler, S. R. *Angew. Chem., Int. Ed.* **2010**, *49*, 6365. (b) Wen, Y.; Zhao, B.; Shi, Y. *Org. Lett.* **2009**, *11*, 2365. (c) Zhao, B.; Du, H.; Shi, Y. *Org. Lett.* **2008**, *10*, 1087. (d) Zhao, B.; Yuan, W.; Du, H.; Shi, Y. *Org. Lett.* **2007**, *9*, 4943.

(9) For related diamination of butadienes using palladium and copper catalysis, see: (a) Bar, G. L. J.; Lloyd-Jones, G. C.; Booker-Milburn, K. I. *J. Am. Chem. Soc.* **2005**, *127*, 7308. (b) Du, H.; Zhao, B.; Shi, Y. *J. Am. Chem. Soc.* **2007**, *129*, 762. (c) Du, H.; Yuan, W.; Zhao, B.; Shi, Y. *J. Am. Chem. Soc.* **2007**, *129*, 7496. (d) Du, H.; Yuan, W.; Zhao, B.; Shi, Y. *J. Am. Chem. Soc.* **2007**, *129*, 11688. (e) Wang, B.; Du, H.; Shi, Y. *Angew. Chem., Int. Ed.* **2008**, *47*, 8224. (f) Du, H.; Zhao, B.; Shi, Y. *J. Am. Chem. Soc.* **2008**, *130*, 8590. (g) Xu, L.; Shi, Y. *J. Org. Chem.* **2008**, *73*, 749. (h) Zhao, B.; Du, H.; Cui, S.; Shi, Y. *J. Am. Chem.*

*Soc.* **2010**, *132*, 3523. (i) Zhao, B.; Du, H.; Shi, Y. *J. Org. Chem.* **2009**, *74*, 8392. (j) Yuan, W.; Du, H.; Zhao, B.; Shi, Y. *Org. Lett.* **2007**, *9*, 2589. (k) Zhao, B.; Du, H.; Shi, Y. *Org. Lett.* **2008**, *10*, 1087. (l) Du, H.; Zhao, B.; Yuan, W.; Shi, Y. *Org. Lett.* **2008**, *10*, 4231. (m) Zhao, B.; Peng, X.; Cui, S.; Shi, Y. *J. Am. Chem. Soc.* **2010**, *132*, 11009. (n) Zhao, B.; Peng, X.; Cui, S.; Shi, Y. *J. Am. Chem. Soc.* **2010**, *132*, 11009. (o) Cornwall, R. G.; Zhao, B.; Shi, Y. *Org. Lett.* **2011**, *13*, 434.

(10) For metal-free diamination, see: (a) Reference 5e. (b) Röben, C.; Souto, J. A.; González, Y.; Lishchynskyi, A.; Muñiz, K. *Angew. Chem., Int. Ed.* **2011**, *50*, 9478.

(11) Muñiz, K.; Streuff, J. P.; Chávez, C. H.; Hövelmann. *Chem. Asian J.* **2008**, *3*, 1248.

(12) Muñiz, K. *Angew. Chem., Int. Ed.* **2009**, *48*, 9412.

(13) See the Supporting Information for details.

(14) Minatti, A.; Muñiz, K. *Chem. Soc. Rev.* **2007**, *36*, 1142.

(15) For leading examples on *syn*-aminopalladation: (a) White, P. B.; Stahl, S. S. *J. Am. Chem. Soc.* **2011**, *133*, 18594. (b) Liu, G. S.; Stahl, S. S. *J. Am. Chem. Soc.* **2006**, *128*, 7179. (c) Liu, G. S.; Stahl, S. S. *J. Am. Chem. Soc.* **2007**, *129*, 6328. (d) Neukom, J. D.; Perch, N. S.; Wolfe, J. P. *J. Am. Chem. Soc.* **2010**, *132*, 6276. (e) Hanley, P. S.; Marković, D.; Hartwig, J. F. *J. Am. Chem. Soc.* **2010**, *132*, 6302. (f) Neukom, J. D.; Perch, N. S.; Wolfe, J. P. *Organometallics* **2011**, *30*, 1269. (g) Hanley, P. S.; Hartwig, J. F. *J. Am. Chem. Soc.* **2011**, *133*, 15661. (h) Wolfe, J. P.; Ney, J. E. *Angew. Chem., Int. Ed.* **2004**, *43*, 3605. (i) Wolfe, J. P.; Ney, J. E. *J. Am. Chem. Soc.* **2005**, *127*, 8644. (j) Wolfe, J. P.; Nakhla, J. S.; Kampf, J. W. *J. Am. Chem. Soc.* **2006**, *128*, 2893. (k) Isomura, K.; Okada, N.; Saruwatari, M.; Yamasaki, H.; Taniguchi, H. *Chem. Lett.* **1985**, 385.

(16) For the conceptual introduction of transient palladium oxidation, see: Stangl, H; Jira, R. *Tetrahedron Lett.* **1970**, *11*, 3589. Hamed, O.; Henry, P. M. *Organometallics* **1998**, *17*, 5184. *Palladium Catalyzed Oxidation of Hydrocarbons*; Henry, P. M., Ed.; Reidel: Dordrecht, 1980.

(17) Chávez Vásquez, P. Ph.D. Thesis, University of Strasbourg, 2011.

(18) Giorgioni, G.; Claudi, F.; Ruggieri, S.; Ricciutelli, M.; Palmieri, G. F.; Di Stefano, A.; Sozio, P.; Cerasa, L. S.; Chiavaroli, A.; Ferrante, C.; Orlando, G.; Glennon, R. A. *Bioorg. Med. Chem.* **2010**, *18*, 1834.